

REMARKS

Applicants request reconsideration on the merits of the above-referenced patent application.

I. Claim status

Claims 1-7 are pending, and claim 8 is withdrawn. This paper does not make any amendments to the claims. Claims 1-8, however, are presented on page 2 for the convenience of the reader.

II. Response to objection to abstract

An objection has been raised to the abstract under MPEP §608.01(b) for containing legal phraseology such as "comprising." Applicants request withdrawal of this objection.

At the outset, Applicants respectfully submit that there is no mandatory requirement that an abstract exclude legal phraseology. To the contrary, MPEP §608.01(b) merely suggests that legal phraseology be avoided:

The form and legal phraseology often used in patent claims, such as "means" and "said," **should** be avoided. (emphasis added).

Thus, Applicants are unaware of any authority that supports an objection to an abstract for containing legal phraseology.

Moreover, Applicants respectfully submit that the term "comprising" is *not* legal phraseology. While "comprising" has been expressly defined by the courts (*see* MPEP §2111.03), that does not make it legal phraseology. If anything, use of a term having such a clear definition recognized by the courts makes the abstract more definite, and, therefore, more understandable.

Ultimately, the purpose of the abstract is to provide "a concise statement of the technical disclosure of the patent." *See* MPEP §608.01(b). Applicants' abstract fulfills this purpose. Substituting alternative language for "comprising" is, therefore, unnecessary. In fact, such substitute language could lead to confusion for not being consistent with the language in the rest of Applicants' specification.

For at least the foregoing reasons, Applicants respectfully submit that the objection must be withdrawn.

III. Response to rejection of claims 1-3 and 7 under 35 USC §103(a)

Claims 1-3 and 7 have been rejected under 35 USC §103(a) as being obvious over Farnsworth ("The effect of penicillin, dihydrostreptomycin and prednisolone treatment of experimental *Candida krusei* infections of the mammary glands of dairy cattle," *Can. J. Comp. Med.*, 39(3), pp. 340-48 (July 1975)) in view of Lohuis ("Effect of steroid anti-inflammatory drugs on *Escherichia coli* endotoxin-induced mastitis in the cow," *J. Dairy Sci.*, 72, pp. 241-49 (1989)). Applicants request withdrawal of this rejection.

A. Claim 1

Claim 1 is directed to a pharmaceutical composition for intramammary administration. The composition comprises an antibacterial agent, prednisolone, and a carrier. The amount of prednisolone is at least 20 mg per unit dose.

As explained in Applicants' specification, Applicants' invention stems from their discovery that the minimum 20 mg prednisolone unit dose provides increased anti-inflammatory efficacy while unexpectedly not increasing immunosuppressive side effects compared to compositions comprising less prednisolone. More specifically, at the time of Applicants' filing, prednisolone was used in combination with antibacterial agents to treat mastitis. As far as Applicants are aware, however, the unit dose of prednisolone in such treatments generally did not exceed 10 mg. *See, e.g.*, Applicants' specification, page 2, line 31 to page 3, line 11. There was, after all, no apparent expectation that greater prednisolone doses would be advantageous. To the contrary, prednisolone was known to have immunosuppressive side effects. The impact of any such side effects could be particularly significant in the context of bacterial-induced mastitis, given that a depressed immune defense could support bacterial growth and, therefore, promote the disease. *See, e.g.*, Applicants' specification, page 3, lines 27-32. It was in this context that Applicants unexpectedly discovered that the greater prednisolone concentration recited in claim 1 generally does not negatively affect the cure rate of bacterial-induced mastitis when administered with an antibacterial agent. *See, e.g.*, Applicants' specification, page 4, lines 11-21; and Examples 4-5 on pages 12-16.

Farnsworth discusses the effects of a prednisolone composition on a *yeast* infection. A unit dose of the studied composition reportedly contained penicillin G, dihydrostreptomycin, and

10 mg of prednisolone. Applicants respectfully submit that Farnsworth fails to provide any teaching or suggestion that renders the composition of claim 1 obvious. Importantly, Farnsworth expressly states that the mammary glands in the study were not infected with bacteria. See Farnsworth, page 348 (first column, lines 12-13). Thus, a skilled artisan looking to develop an antibacterial composition to treat mastitis would not look to Farnsworth. Moreover, Farnsworth fails to provide any teaching or suggestion as to the effect of prednisolone or changes in its concentration. Farnsworth, in fact, expressly states that the effect of prednisolone could not be evaluated in the study. See Farnsworth, page 348 (first column, lines 34-40). If anything, Farnsworth corroborates Applicants' contention that a 10 mg prednisolone unit dose was typical in mastitis treatments at the time of Applicants' filing. See Farnsworth, pages 342 (first column, lines 55-59) and 348 (first column, lines 28-30). Such a teaching would have steered a skilled artisan away from using the higher concentration recited in Applicants' claim 1, further evidencing the *non*-obviousness of claim 1. See MPEP §2145(X)(D)(1) (a prior art reference that "teaches away" from the claimed invention is a significant factor to be considered in determining obviousness). Thus, for at least the foregoing reasons, Farnsworth alone fails to support a *prima facie* showing of obviousness against Applicants' claim 1.

Lohuis discusses the effects of a 40 mg unit dose of prednisolone in *E. coli* endotoxin-induced mastitis. In this study, no antibacterial agent was co-administered. At the outset, Lohuis did not study the use of prednisolone to treat an actual bacterial infection — it only studied mastitis caused by endotoxins. Lohuis, in fact, acknowledges that it is unclear whether its reported effects of the prednisolone could be reproduced in the context of an actual bacterial infection. See Lohuis, page 248 (column 1, lines 48-51). Moreover, because Lohuis' prednisolone composition does not contain antibacterial agent, Lohuis fails to teach or suggest any composition that could be used to cure mastitis caused by a bacterial infection. Thus, a skilled artisan, seeking a *cure* to mastitis caused by a bacterial infection, would not turn to Lohuis. Even more, Luhuis fails to provide any teaching or suggestion that would allow a skilled artisan to predict whether the immunosuppressive effects of a 40 mg prednisolone unit dose would promote bacterial growth if used to treat an actual bacterial infection, particularly when such a unit dose is co-administered with an antibacterial agent. Thus, for at least the

foregoing reasons, Lohuis alone fails to support a *prima facie* showing of obviousness against Applicants' claim 1.

Even if combined, Farnsworth and Lohuis fail to support a *prima facie* showing of obviousness against Applicants' claim 1. First off, neither reference studies the treatment of an actual bacterial infection --- Farnsworth limited its study to yeast infections, and Lohuis limited its study to mastitis caused by endotoxins. Thus, a skilled artisan, looking to develop a composition to treat a bacterial infection, would not have turned to these references. Moreover, a finding of *prima facie* obviousness requires a finding that the cited references would have provided a skilled artisan with a *reasonable expectation of success*. See MPEP 2143.02.

Farnsworth and Lohuis could not have provided such an expectation with respect to Applicants' composition in claim 1. As noted above, prednisolone was known to have immunosuppressive side effects. The cited references, even when combined, fail to provide any teaching or suggestion that would have allowed a skilled artisan to reasonably expect that the prednisolone concentration in claim 1 could be advantageous without having immunosuppressive side effects deleterious to the antibacterial cure rate. If anything, the cited references corroborate Applicants' contention that a 10 mg prednisolone unit dose was typical for treating mastitis caused by bacterial infections. This teaching would have steered a skilled artisan toward using the 10 mg dose, and, therefore, away from the higher concentration of claim 1. The cited references, therefore, cannot support a *prima facie* showing of obviousness even when combined.

For at least the foregoing reasons, Applicants respectfully submit that the rejection must be withdrawn.

B. Claims 2, 3, and 7

Claims 2, 3, and 7 directly or indirectly depend from claim 1, and, therefore, are patentable over the cited references for at least the same reasons as claim 1.

IV. Response to rejection of claims 4-6 under 35 USC §103(a)

Claims 4-6 have been rejected under 35 USC §103(a) as being obvious over Farnsworth in view of Lohuis and in further view of Hornish ("Cephalosporins in veterinary medicine ---

Ceftiofur use in food animals," *Current Topics in Medicinal Chemistry*, 2(7), pp. 717-731 (2002)). Applicants request withdrawal of this rejection.

A. Claim 4

Claim 4, like claim 1, is directed to a pharmaceutical composition for intramammary administration. The composition comprises an antibacterial agent, prednisolone, and a carrier. The amount of prednisolone is at least 20 mg per unit dose. In claim 4, the antibacterial agent is cephalosporin.

Because claim 4 depends from claim 1, it is necessarily patentable over Farnsworth and Lohuis for at least the same reasons as claim 1. This conclusion of patentability remains the same even if Farnsworth and Lohuis are combined with Hornish. More specifically, Hornish is simply cited for its discussion related to using cephalosporins to treat mastitis infections. Hornish fails to cure the deficiencies of Farnsworth and Lohuis discussed above.

Hornish, for example, fails to discuss any compositions containing prednisolone (or any other corticosteroid or anti-inflammatory agent). Consequently, all three references fail to teach, suggest, or provide motivation for developing a composition having the prednisolone concentration of claim 4 to treat mastitis caused by a bacterial infection. If anything, Hornish's failure to even mention the use of prednisolone (or any other corticosteroid or anti-inflammatory agent) arguably would have steered a skilled artisan away from the composition of claim 4 by suggesting that prednisolone is unnecessary (or perhaps even undesirable) for the antibacterial compositions discussed in Hornish.

Hornish also fails to provide any teaching or suggestion that would have caused a skilled artisan to believe that the prednisolone concentration in claim 4 could be advantageous without being deleterious to the antibacterial cure rate. As noted above, Hornish does not mention the use of prednisolone or any other anti-inflammatory agent. Consequently, all three cited references fail to provide any teaching or suggestion that would have provided a reasonable expectation of success in advantageously using the prednisolone concentration of claim 4 without immunosuppressive side effects deleterious to the antibacterial cure rate.

Thus, for at least these reasons, the cited references, even with Hornish, fail to support a *prima facie* showing of obviousness with respect to claim 4.

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B. Claims 5 and 6

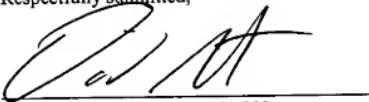
Claims 5 and 6 depend from claim 4, and, therefore, are patentable over the cited references for at least the same reasons as claim 4.

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Applicants hereby request a two-month extension to respond to the November 9, 2007 Office action, and authorize the Commissioner to charge the fee for that extension to Deposit Account No. 02-2334. Applicants do not believe that any other fee is due in connection with this filing. If, however, Applicants do owe any such fee(s), the Commissioner is hereby authorized to charge the fee(s) to Deposit Account No. 02-2334. In addition, if there is ever any other fee deficiency or overpayment under 37 C.F.R. §1.16 or 1.17 in connection with this patent application, the Commissioner is hereby authorized to charge such deficiency or overpayment to Deposit Account No. 02-2334.

Applicants submit that this application is in condition for allowance, and request that it be allowed. The Examiner is requested to call the Undersigned if any issues arise that can be addressed over the phone to expedite examination of this application.

Respectfully submitted,



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